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In the context of adaptive radiation therapy, we have validated algorithms for automatic organ segmentation, and demonstrated techniques for calculating dose actually delivered. Both procedures depended on methods for deformably registering CT images taken during treatment to the planning image. A statistical analysis comparing the automatic segmentation to two human segmenters showed that the automatic method was within the range of human variation. We have also applied our dose accumulation method to a number of patient data sets, using a variety of planning assumptions.

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Introduction

The goal of this research is to develop automated methods to analyze daily CT scans taken during prostate therapy, in order to make adaptive radiation therapy (ART) more effective and readily implemented. The central technique is deformable image registration, which allows a CT image acquired for treatment planning to be deformed to match each daily image. The resulting deformations can then be applied to contours drawn at planning time, to generate segmentations of treatment images. Inverse deformations can also be applied to dose distributions (represented as images indicating the dose delivered to each voxel). In this way, the dose distributions can be deformed into the reference frame of the planning image, and summed over the course of treatment to determine the total delivered dose. Over the past year we have demonstrated both of these techniques on data from multiple subjects. We have published our findings in the Journal Physics in Medicine and Biology. The paper

Body

Task 1: Validation of Automatic Segmentation

We performed a statistical validation of our algorithm by performing segmentation on 48 treatment images from four patients. We found that automatic segmentations derived (by deformation) from one individual's planning contours matched that individual's later segmentations at least as well as did segmentations by a different individual. Our analysis was based on two measures of geometric variation, centroid difference and volume overlap. Extensive details of this work are given in three related papers, included as Appendices A and B and C. With this work, all portions of Statement of Work have been addressed: The algorithms accommodate rectal filling, dealing in particular with the severe problems caused by gas (1a). We have developed and applied methodologies to validate the algorithms.
We have successfully recruited over 20 subjects each with multiple intra treatment images. The performance of the algorithm has been analyzed using the collected data sets.

Task 2: Develop and validate methodology that uses the organ deformation estimates provided by the image mapping algorithms to compute actual delivered dose via dose accumulation techniques

The ability to transform the distribution of dose from one treatment day to the planning day, and then accumulate such doses from different days, makes it possible to analyze how the motion of an actual patient would affect a treatment plan for that patient. It is thus possible to test novel treatments against motion data from patients that have already been treated, in what we call a virtual clinical trial.

When delivered dose is accumulated, the doses delivered to each voxel can simply be summed over the range of treatments. However, it is also possible to apply models that take into account the effect of fraction size on the biological effectiveness of a dose. We have used the linear-quadratic model, as described in Appendix B.

As a baseline, and to illustrate this concept of dose accumulation, for nine subjects we have evaluated the total delivered dose to the prostate and rectum assuming that no adaptive radiation therapy had been used. The results are shown in Figure 1, and were presented as a poster at the meeting of the American Society of Therapeutic Radiology and Oncology (ASTRO). For the prostate, we computed prescribed and delivered EUD, and delivered mean dose. For the rectum, we computed the percent of the volume receiving more than 65 Gy, and also the percent receiving more than 40 Gy. These values can be compared to prescribed values of 78 for the dose, no more than 17% of the rectum to receive more than 65 Gy, and no more than 35% to receive more than 40 Gy.

Task 3) Develop and validate algorithms to determine the significance of ART protocols in delivered dose by performing dosimetric comparisons using models of *equivalent uniform dose* (EUD) *tumor control probability* (TCP) and *normal tissue complication probability* (NTCP.),

As an illustration of the concept of a virtual clinical trial, for three patients we have computed DVHs of delivered BED using the linear-quadratic model. We used α/β values of 1.5 for the prostate and 4 for the rectum [Brenner 2003]. The patients had been treated with a conventional course of 39 fractions at 2 Gy per fraction. For comparison, we simulated a hypofractionation plan with 15 fractions of 3 Gy each. Using the deformation fields computed for the patients, we computed delivered BED for 15 fractions (using the first 15 imaged treatments for each patient), and compared it to the planned BED for the hypothetical hypofractionation plan, along with the planned BED for the plan actually used.

Key Research Accomplishments

- Comparison of manual segmentation with our automatic method, using several measures, indicating that automatic segmentations derived from one individual's planning segmentation match that person's later segmentations at least as well as manual segmentations by a different rater.
- Computation of the actual cumulative dose delivered to both the cancerous and critical healthy tissues of nine subjects.
- Dose volume histograms of BED using the linear-quadratic model for three subjects.
- Publication of the Article in *Physics in Medicine and Biology*: "Large deformation 3D image registration in image-guided radiation therapy," by Mark Foskey, Brad Davis, Lav Goyal, Sha Chang, Ed Chaney, Nathalie Strehl, Sandrine Tomei, Julian Rosenman, and Sarang Joshi. Included here as Appendix B.

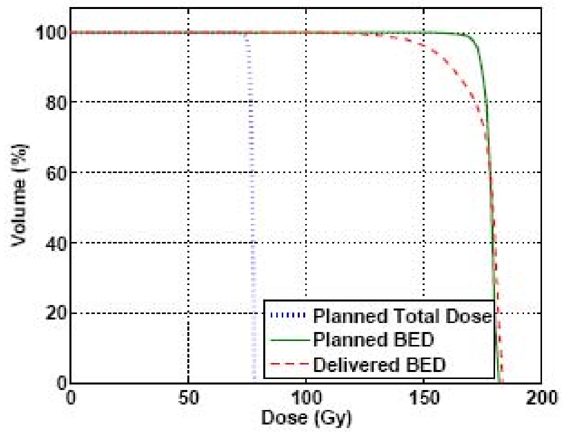

Figure 14. DVHs for Planned total dose, planned BED, and delivered BED. Delivered BED is modeled from a sample of 18 out of 39 treatment days. $\alpha/\beta = 1.5$.

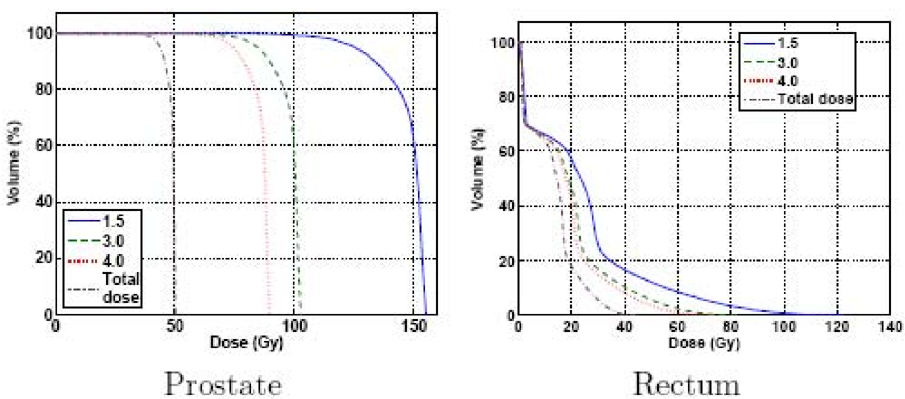

Figure 1. BED for prostate, bladder and rectum. Planned BED is compared to calculated delivered BED for a treatment of 15 fractions at 3 Gy/f, and also to the planned BED for a conventional 39 x 2 plan.

Reportable Outcomes

Abstracts:

M. Foskey, B. Davis, L. Goyal, S. Chang, J. Rosenman, and S. Joshi. "Calculating biological effective dose in the presence of organ deformation." AAPM 47th Annual Meeting, 2005.

K. Wijesooriya, V. Dill, L. Dong, R. Mohan, S. Joshi, E. Weiss, and P. Keall. "Comparison of auto contouring with manual contouring: A first step towards automated 4D treatment planning." AAPM 47th Annual Meeting, 2005.

M. Foskey, B. Davis, L. Goyal, S. Chang, J. Rosenman, and S. Joshi. "Automatic contouring via deformable image registration." ASTRO, 2005.

Full Length Conference Papers:

B. Davis, M. Foskey, J. Rosenman, L. Goyal, S. Chang, S. Joshi. "Automatic segmentation of intra-treatment CT images for adaptive radiation therapy of the prostate." *Proceedings of MICCAI*, 2005. Included here as appendix A.

Journal Papers:
Foskey M, Davis B, Goyal L, Chang S, Chaney E, Strehl N, Tomei S, Rosenman J, Joshi , Large deformation three-dimensional image registration in image-guided radiation therapy. Phys Med Biol 2005 Dec 21;50(24):5869-92 Included as appendix B.

Conclusions

Over the course of the Grant we have accomplished all the specific aims of the project. We have Developed and validate deformable image mapping algorithms to automatically quantify the daily anatomical variation of the prostate and the neighboring radiosensitive normal structures in intra-treatment CT images. The inclusion of Bowel Gas in the rectum was a major advancement in the field of deformable image registration.
2) Using these deformable image mapping algorithms to calculate actual delivered dose to the prostate and nearby organs accommodating motion and setup variability.
3) Perform dosimetric evaluations by comparing conventionally planned and ART-planned treatments with the actually delivered dose distribution using various dose-volume metrics.

All of these methods were published in the journal article: "Large deformation three-dimensional image registration in image-guided radiation therapy". Phys Med Biol 2005 Dec 21;50(24):5869-92

We have also extended these methods to the tracking of organs during breathing. This work was not part of the originally proposed Grant but was an unexpected by product. These methods were reported in:

Pevsner A, Davis B, Joshi S, Hertanto A, Mechalakos J, Yorke E, Rosenzweig K, Nehmeh S, Erdi YE, Humm JL, Larson S, Ling CC, Mageras G , Evaluation of an automated deformable image matching method for quantifying lung motion in respiration-correlated CT images. Med Phys 2006 Feb;33(2):369-76